Sequential Femoral Distal Composite Bypass with Second Generation Glutaraldehyde Stabilized Human Umbilical Vein (HUV)

Neufang A, Espinola-Klein C, Dorweiler B, et al. Eur J Vasc Endovasc Surg 2005;30:176-83.

Conclusion: Limb salvage and graft patency rates with sequential composite bypasses composed of second generation human umbilical vein grafts and autogenous vein provide reasonable primary and secondary patency rates and are associated with excellent limb salvage.

Summary: The authors sought to evaluate a policy of using a combination of second generation human umbilical vein (HUV) grafts and autogenous vein as a sequential conduit in patients felt to have inadequate autogenous conduit for construction of an all autogenous lower extremity bypass. This was a retrospective study from a single center in Germany. From January 1998 to December 2003, 1,231 infrainguinal bypasses were performed in this center. Of those, 54 consisted of a femoral-distal HUV-autologous vein sequential composite bypass. All patients had critical leg ischemia and were felt to have an absence of sufficient length of autogenous vein. The sequential HUV-composite technique was reviewed for graft patency, limb salvage, and patient survival.

Primary and secondary patency rates at 1, 2, 3 and 4 years were 71, 61, 53 and 53%, and 89, 80, 73 and 67% respectively. Limb salvage rates at 1, 2, 3, and 4 years were 96, 92, 88 and 88%. Four year survival was 56%. After one month, additional graft based procedures were required in six bypasses. Five patients had asymptomatic occlusion of one sequential anastomosis. There were no identified complications related to bio-degeneration of the HUV graft.

Comment: There still remains some interest in the use of human umbilical vein grafts. The author's technique of using human umbilical vein grafts as the prosthetic component of a prosthetic/autologous sequential composite bypass has provided reasonable results in terms of both patency and limb salvage. The results differ little from what one would expect with similar procedures with PTFE grafts. Bio-degeneration of the HUV grafts in this series of limb salvage patients appeared to be a non issue. If a sequential composite autogenous graft is required it appears to make little difference whether the prosthetic component is PTFE or human umbilical vein.

Immediate and 1-Year Outcome of Percutaneous Intervention of Saphenous Vein Graft Disease with Paclitaxel-Eluting Stents

Tsuchida K, Ong ATL, Aoki J, et al. Am J Cardiol 2005;96:395-8.

Conclusion: Implantation of paclitaxel-eluting stents in stenotic coronary artery bypass saphenous vein grafts is feasible and safe with a low rate of re-intervention at one year.

Summary: In native coronary arteries drug eluting stents dramatically reduce restenosis following percutaneous angioplasty. This study reports the use of paclitaxel-eluting stents in the treatment of stenotic lesions of coronary saphenous vein grafts. Between February and December of 2003, the authors performed interventions in 50 consecutive patients with 62 coronary vein graft lesions. Two patients died immediately of cardiogenic shock and eight patients received bare metal stents due to unavailability of appropriately sized paclitaxel-eluting stents. Overall, there were 40 consecutive patients with 52 coronary vein graft lesions who were treated electively with paclitaxel-eluting stents. All patients received a loading dose of 300 mgs of clopidogrel followed by 75 mgs of clopidogrel per day for six months. They were subsequently maintained on life long aspirin. In addition, heparin, with an activated clotting time of greater than 250 seconds, was utilized during the stent implantation procedure. Thrombectomy devices or glycoprotein 2B/3A inhibitors were used at the discretion of the interventional cardiologist. Patients were followed and evaluated for survival using Kaplan-Meier analysis. End points were major adverse cardiac events (MACE) and were defined as death, myocardial infarction, target lesion revascularization or target vessel revascularization. During followup, one patient (2.5%) had a non Q-wave MI as an in-hospital complication. No patient died and the cumulative MACE rate was 7.5%, with a one year event free survival of rate of 92.5%.

Comment: It appears coronary vein grafts can be successfully treated with paclitaxel-eluting stents with associated favorable short term clinical follow-up. (No angiographic follow-up was presented in this study.) The different flow characteristics of peripheral saphenous vein grafts versus coronary grafts are obvious. Therefore, this data cannot be used to justify treatment of peripheral saphenous vein grafts with drug eluting stents. However, the results are certainly intriguing and it is only a matter of time before drug eluting stents will be placed in peripheral vein grafts.

Efficacy and Safety of Edifoligide, an E2F Transcription Factor Decoy, For Prevention of Vein Graft Failure Following Coronary Artery Bypass Graft Surgery, Prevent IV: A Randomized Control Trial

Prevent IV Investigators. JAMA 2005;294:2446-54.

Conclusion: The E2F decoy edifoligide does not prevent angiographic vein graft failure at 12 to 18 months following coronary artery bypass surgery.

Summary: E2F transcription factors up regulate genes believed to play a role in intimal hyperplasia. The E2F decoy edifoligide may prevent neointimal hyperplasia and subsequent vein graft failure by inhibiting up regulation of the E2F transcription factors implicated in neointimal hyperplasia.

This was a Phase 3 randomized, double blind, placebo controlled trial of patients undergoing first time coronary artery bypass surgery and who had at least two planned saphenous vein grafts. There were 107 U.S. sites involved in the study. Vein grafts were treated ex vivo with either placebo or the E2F decoy. Angiographic followup was at 12-18 months in the first 2,400 patients enrolled in the study. The primary end point was angiographic vein graft stenosis (>75%) at 12-18 months following CABG. Also recorded were adverse events through 30 days and major cardiac adverse events.

There were 1,920 patients who either died (n = 91) or underwent followup angiography (n = 1,829). The primary end point was reached in 436 of 965 patients in the edifoligide group (45.2%) and in 442 of 995 patients in the placebo group (46.3%). (Odds ratio: 0.96 [95% CI, 0.8-1.14], p = 0.66). There was also no effect on any secondary angiographic end point or major cardiac events at one year (6.7% of 1,508 patients in the edifoligide group versus 8.1% of 1,506 patients in the placebo group, Hazard ratio 0.83, 95% CI, 0.64-1.08; p = 0.16).

Comment: This study, along with Prevent III, which also failed to show benefit of edifoligide in preventing vein graft failure for peripheral arterial reconstructions, provides conclusive evidence as to the ineffectiveness of edifoligide in preventing neointimal hyperplasia. It is now known, however, that the E2F family of transcription factors contains at least eight unique E2F transcription factors. (Journal Biologic Chemistry 2005;280: 18211-20). Some of these transcription factors inhibit neointimal hyperplasia while others appear to promote neointimal hyperplasia. Edifoligide inhibits the entire E2F family and therefore failure of the apparent "shotgun" approach employed in Prevent III and Prevent IV was perhaps inevitable. Future research in this area will need to focus on effects of specific E2F transcription factor decoys.

Nitric Oxide Modulates Vascular Inflammation in Intimal Hyperplasia and Insulin Resistance in the Metabolic Syndrome

Barbato JE, Zuckerbraun BS, Overhaus, M, et al. Am J Physiol Heart Circ Physiol 2005;289:H228-36.

Conclusion: Inducible nitric oxide synthase (iNOS) gene transfer can inhibit the arterial injury response and reduce neointimal formation.

Summary: Both the metabolic syndrome and Type II diabetes mellitus are characterized by insulin resistance. Both are associated with atherosclerotic vascular disease and may have increased risk of poor outcome following vascular intervention. The vascular events associated with Type II diabetes mellitus and the metabolic syndrome may be related to reduced bioavailability of nitric oxide (NO) and a heightened inflammatory environment. The authors sought to characterize the vascular injury response in diabetes and the metabolic syndrome by studying obese Zucker rats and examining expression of adhesion molecules, development of intimal hyperplasia, and recruitment of inflammatory cells. The ability of exogenous NO to inhibit the vascular injury response in the metabolic syndrome was also studied.

Both lean and obese Zucker rats were subject to a carotid artery balloon injury model. P-selectin and ICAM-1 expression was increased following balloon injury in obese animals compared to lean ones. The obese rats had increased macrophage infiltration of the vascular wall and increased neointimal formation compared to lean animals (intima/media = 0.91 v 0.52, $P = 0.001$). There was a significant reduction in ICAM-1, P-selectin, inflammatory cell influx and oxidized LDL receptor expression following adenovirus-mediated inducible NO synthase (iNOS) gene transfer. Proliferative activity was also significantly reduced by iNOS gene transfer (54% and 73%; $P < 0.05$). Neointimal formation was also reduced in lean versus obese rats (53% and 67%; $P < 0.05$) with iNOS gene transfer.

Comment: It is known that the vascular injury response and insulin resistant states are characterized by increased adhesion molecule expression. The authors gene based method of delivering iNOS appeared to significantly inhibit adhesion molecule expression. The findings suggest that increasing NO bioavailability may reduce the augmented inflammatory response and oxidative stress characteristic of insulin resistance and vascular injury.